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Low-value clinical practices in adult traumatic brain injury: an umbrella review protocol

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LOW-VALUE CLINICAL PRACTICES IN ADULT TRAUMATIC BRAIN INJURY: AN UMBRELLA REVIEW PROTOCOL

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Running head: Umbrella review on low-value practices in acute TBI care

ABSTRACT

Introduction: Traumatic brain injury (TBI) leads to 50,000 deaths, 85,000 disabilities and costs $60 billion each year in the USA. Despite numerous interventions and treatment options, the outcomes of TBI have improved little over the last three decades. In a previous scoping review and expert consultation survey, we identified 15 potentially low-value clinical practices in acute TBI. The objective of this umbrella review is to synthesize the evidence on potentially low-value clinical practices in the care of acute TBI.

Methods and analysis: Using umbrella review methodology, we will search Cochrane CENTRAL, EMBASE, Epistemonikos, PROSPERO and PubMed to identify systematic reviews evaluating the effect of potential intra-hospital low-value practices. We will present data on the methodological quality of these reviews (AMSTAR-2), reported effect sizes and the strength of evidence (GRADE).

Ethics and dissemination: Ethics approval is not required as original data will not be collected. Knowledge users from five healthcare quality organisations and clinical associations are involved in the design and conduct of the study. Results will be disseminated in a peer-reviewed journal, at international scientific meetings and to clinical, healthcare quality and patient-partner associations. This work will support the development of metrics to measure the use of low-value practices, inform policy makers on potential targets for de-implementation, and in the long term reduce the use of low-value clinical practices in acute TBI care.

Registration details: The protocol is currently under evaluation with the International Prospective Register of Systematic Reviews (PROSPERO).

STRENGTHS AND LIMITATIONS OF THIS STUDY

- State-of-the-art synthesis of evidence on low-value clinical practices in the care of acute TBI
- Represents a crucial step towards the de-implementation of low-value practices in acute TBI care
- Adopts an integrated knowledge translation model to ensure the results are relevant to decision makers
- For feasibility reasons, our synthesis is restricted to systematic reviews published in English since 1990
- The scope of review and the inclusion of systematic reviews precludes meta-analysis

INTRODUCTION

Traumatic brain injury (TBI) is the main cause of mortality from injury in people under 45 years of age[1] and it leads to approximately US$60 and €33 billion in total medical costs in the USA[2] and Europe[3] each year, respectively. Moreover, outcomes following TBI have not improved significantly in the last four decades.[4, 5] Intervention and treatment options for TBI are multiple, but many lack robust evidence of their effectiveness.[6, 7]

Low-value clinical practices, defined as a test or procedure that is not supported by evidence and/or could expose patients to unnecessary harm [8-15] consume up to 30% of healthcare budgets.[9, 16] In the past decade, the medical community has turned towards the de-implementation of low-value practices as a promising means to reduce the strain on healthcare budgets, free-up resources and reduce harm to patients.[17] Physicians report using low-value practices because of a lack of alternative treatment options, fear of legal consequences but also because of lack of guidelines on low-value care.[15, 18] The *Brain Trauma Foundation*, among others, publish guidelines on TBI care.[19] However, emphasis is on practices that should be adhered to rather than practices that should be avoided. *Choosing Wisely* publish recommendations specifically targeting low-value practices but few pertain to TBI care and many are based uniquely on expert consensus.[11] A previous scoping review and expert consultation survey identified 13 potentially low-value clinical practices in acute TBI care.[20] These practices represent potential targets for guidelines, overuse metrics and de-implementation interventions. However, before recommendations can be made, we need to synthesize the evidence base for these practices.

Interventions and treatment options for acute TBI have been the subject of multiple systematic reviews.[21, 22] Given this large body of available evidence, evidence maps have previously been used to summarize evidence from systematic reviews on acute TBI interventions.[7, 23] However, these evidence maps were not designed to target low-value practices and focused on moderate to severe TBI when the mild TBI population represent great potential for reducing low-value care. In addition, previous reviews have not provided a synthesis of effect sizes or strength of evidence. The objective of the present study is to synthesize the evidence on potentially low-value intra-hospital clinical practices in acute adult TBI.

METHODS AND ANALYSIS

Given the multitude of systematic reviews available for the clinical practices identified as potentially low-value (over 60 were identified in our scoping review), we opted to conduct an umbrella review,[20] The review will be conducted according to published guidelines.[24-26] In the absence of reporting guidelines for umbrella reviews, we will use the applicable Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P).[27] The protocol is currently under evaluation with the International Prospective Register of Systematic Reviews (PROSPERO).

Eligibility criteria

The project steering committee comprising clinicians (2 emergency physicians, 7 critical care physicians, 1 neurosurgeon), methodologists (4), and health system managers (3) used the population, intervention, comparator, outcome and study design (PICOS) framework to develop specific research questions for each potentially low-value clinical practice (Table 1).[20, 28] We will consider systematic reviews of original studies evaluating the effectiveness of pre-determined clinical practices in acute TBI in adults (≥ 16 years old), without restriction on location of publication but limited to studies published in English since 1990.[25, 26]

We will use the Cochrane definition to identify systematic reviews. We will consider a review to be systematic if it clearly stated a set of objectives and reported explicit eligibility criteria, an extensive search strategy (a refined search strategy ran on MEDLINE or Cochrane Library and at least one other database)[29, 30] and reproducible methods to identify, select, and critically appraise the findings of the included studies.[24]

Outcomes

Primary and secondary outcomes were identified for each of the evaluated clinical practices by the project steering committee and are described in a PICO format in Table 1.

Search strategy

In consultation with an information specialist, we will develop comprehensive literature search strategies separately for each clinical practice to be studied (see Table 2 for a preliminary search

strategy in PubMed). We will search systematic reviews using the Cochrane Library, Excerpta Medica Database (EMBASE), Epistemonikos,[31] PubMed and the International Prospective Register of Systematic Reviews (PROSPERO)[32] from 1990 to up to six months prior to submission for publication. Using a snowball approach, we will screen the references of included studies in addition to previous reviews on this subject.[7, 21-23, 33]

Selection process

We will manage all citations with EndNote software (version X8.2, Clarivate Analytics, 2014). We will identify and remove duplicates using electronic and manual screening.[34] To ensure reliability when selecting studies for a given practice, two sets of 100 citations will independently be evaluated and then discussed by the reviewers. Pairs of reviewers (PAT, LM, IF, KMB) will then independently screen all identified records using titles, abstracts and full texts, consecutively. Any disagreement will be resolved through discussion between reviewers and, if necessary, consultation with a senior author (AFT). Potentially eligible studies excluded using full texts will be described in a PRISMA flow chart.

Data items and abstraction process

Using a standardized data abstraction form piloted on a representative sample of 5 studies, pairs of experienced reviewers (PAT, LM, IF, KMB) will independently extract the following data: first author, title, year of publication, databases used and date of the last search; population(s), intervention(s), comparator(s), outcome(s) and study designs included; measures of association and their respective measure of heterogeneity; tools used to assess the quality (risk of bias) of original studies and overall rating from the authors. Any disagreement will be resolved through discussion between reviewers and, if necessary, consultation with a senior author (AFT). When information is available in figures only, we will abstract graphical data using computer-assisted software.[35, 36] Furthermore, we will contact study authors (up to three email attempts) when information is unclear or unavailable.

Methodological quality assessment

Two reviewers (PAT, LM) will independently critically appraise the quality of systematic reviews using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR-2) tool.[37] Methodological quality will be categorised as low (0-3), medium (4-7) and high (8-11).

Level of evidence

Strength of recommendations will be assessed independently by pairs of content experts using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool for diagnostic[38] or therapeutic[39] procedures.

Synthesis

Results will be presented according to current recommendations for umbrella reviews.[40] For each low-value practice, we will present the number of reviews (and patients) included, the quality of the reviews (AMSTAR-2), effect sizes for primary and secondary outcomes (forest plots) and strength of recommendations (GRADE).

Potential limitations

To ensure the feasibility of the review, we will restrict our search to low-value practices identified in the scoping review and expert consultation study, which may lead us to miss some low-value practices. However, given the robust search strategy used in our scoping review and the fact that experts were asked to add any other practices they considered low-value, it is unlikely that important low-value practices have been missed. By targeting systematic reviews rather than original studies, we may miss some evidence. However, given the availability of high-quality, up-to-date reviews in TBI care suggested by our scoping review, we think it unlikely that we will miss a large body of evidence. For certain clinical practices, we may not identify any high-quality, up-to-date reviews. These practices will be the subject of systematic reviews in subsequent phases of the research program. Finally, for feasibility reasons, we limited this umbrella review to reviews published in English since 1990 as per recommendations for umbrella reviews.[25, 26] These limitations should have negligible impact on results since few systematic reviews were published prior to 1990 and most published reviews are likely to be written in English.[25, 26]

Potential impact

This review is part of the *Canadian Program on Monitoring Low-Value Clinical Practices in Injury Care* (Canadian Institutes of Health Research #113664), aiming to evaluate the effectiveness of an audit-feedback module targeting low-value clinical practices in acute injury care. The results of this review will be used to inform the development of quality indicators to be integrated in the audit-feedback module.

We will use state-of-the-art methods to optimize the sensitivity of our search strategy and the robustness of results. Results will be synthesized graphically. Ultimately, this research will inform the development of metrics, guidelines and de-implementation interventions, all targeting low-value injury care. The reduction of low-value clinical practices in acute TBI care has the potential to reduce pressure on strained healthcare budgets, free up resources, reduce adverse events and improve patient outcomes.

ETHICS AND DISSEMINATION

Ethics approval is not required as original data will not be collected. This study will be disseminated in a peer-reviewed journal, international scientific meetings, to knowledge users through clinical and healthcare quality associations (Choosing Wisely Canada, Trauma Association of Canada, American College of Surgeons – Committee on Trauma, International Federation of Emergency Medicine, Institut national d'excellence en santé et en services sociaux, Brain Trauma Foundation) and to patient partners associations (Brain Injury Canada).

Patient and Public Involvement

No patient or public representatives will be involved in this study.

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Tables

Table 1. PICOS for each clinical practice

#	Clinical practice
	Mild traumatic brain injury
1	*Population*: adults with acute mild traumatic brain injury *Intervention*: validated clinical decision rule (e.g. CCHR, CHIP, NEXUS II, NOC) *Comparator*: none *Primary Outcome*: false negative rate (intracranial injury, neurosurgical intervention) *Secondary Outcomes*: sensitivity, specificity *Study design*: systematic review
2	*Population*: adults with acute mild complicated traumatic brain injury *Intervention*: routine repeat head CT in absence of neurological deterioration *Comparator*: none or no repeat head CT in absence of neurological deterioration *Primary Outcome*: progression of intracranial injury *Secondary Outcomes:* neurosurgical intervention, mortality, change in management, hospital length of stay *Study design*: systematic review
3	*Population*: adults with acute mild traumatic brain injury and on anticoagulant and/or antiplatelet therapy *Intervention*: : routine repeat head CT in absence of neurological deterioration *Comparator*: none or no repeat head CT in absence of neurological deterioration *Primary Outcome*: progression of intracranial injury *Secondary Outcomes:* neurosurgical intervention, mortality, change in management, hospital length of stay *Study design*: systematic review
4	*Population*: adults with acute mild traumatic brain injury who are negative on head CT *Intervention*: neurosurgical consultation *Comparator*: none or no neurosurgical consultation *Primary Outcome*: hospital admission *Secondary Outcomes:* neurosurgical intervention, mortality, ICU admission, repeat head CT, hospital length of stay *Study design*: systematic review
5	*Population*: adults with acute mild complicated traumatic brain injury who are not on irreversible anticoagulation *Intervention*: intensive care unit admission

	Comparator: admission to regular ward or step-down unit *Primary Outcome*: neurological/medical decline, neurosurgical intervention *Secondary Outcomes:* medical interventions, mortality, adverse events, hospital length of stay, discharge destination *Study design*: systematic review
	Moderate and severe traumatic brain injury
6	*Population*: adults with acute traumatic brain injury on antiplatelet therapy *Intervention*: platelet transfusion *Comparator*: no platelet transfusion *Primary Outcome*: GOS or GOS-E *Secondary Outcomes:* mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review
7	*Population*: adults with basal skull fractures without evidence of cerebrospinal fluid leakage *Intervention*: antibiotic prophylaxis *Comparator*: no antibiotic prophylaxis *Primary Outcome*: meningitis (confirmed by lumbar puncture) *Secondary Outcomes:* GOS or GOS-E, mortality, surgical correction in patients with CSF leakage, non-CNS infection, hospital and ICU length of stay *Study design*: systematic review
8	*Population*: adults with acute traumatic brain injury and no refractory intracranial hypertension *Intervention*: therapeutic hypothermia *Comparator*: no therapeutic hypothermia *Primary Outcome*: GOS or GOS-E *Secondary Outcomes:* intracranial pressure, mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review
9	*Population*: adults with acute traumatic brain injury *Intervention*: antibiotic prophylaxis for external ventricular drain placement *Comparator*: no antibiotic prophylaxis *Primary Outcome*: ventriculostomy-related infection *Secondary Outcomes:* GOS, mortality, hospital and ICU length of stay *Study design*: systematic review
10	*Population*: adults with acute traumatic brain injury and no refractory intracranial hypertension *Intervention*: neuromuscular blocking agents

	Comparator: no neuromuscular blocking agents *Primary Outcome*: GOS or GOS-E *Secondary Outcomes:* intracranial pressure, mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review
11	*Population*: adults with acute traumatic brain injury *Intervention*: plasma transfusion *Comparator*: no plasma transfusion *Primary Outcome*: GOS or GOS-E *Secondary Outcomes:* mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review
	Severe traumatic brain injury
12	*Population*: adults with acute severe traumatic brain injury *Intervention*: albumin *Comparator*: any other colloid-containing fluids (dextrans, modified gelatins, hydroxyethyl starches) or isotonic crystalloid fluids (saline 0.9% and balanced salt solutions such as compound sodium lactate, Plasma-Lyte) *Primary Outcome*: GOS or GOS-E *Secondary Outcomes:* mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review
13	*Population*: adults with acute severe traumatic brain injury *Intervention*: antiseizure prophylaxis (levetiracetam or phenytoin) >1 week *Comparator*: antiseizure prophylaxis <1 week or no antiseizure prophylaxis *Primary Outcome*: late post-traumatic seizure *Secondary Outcomes:* GOS or GOS-E, mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review

CCHR, Canadian Computed Tomography Head Rule; CHIP, Computed Tomography in Head Injury Patients; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; GOS, Glasgow Outcome Scale; ICU, intensive care unit; NEXUS, National Emergency X-Radiography Utilisation Study; NOC, New Orleans Criteria

Table 2. Search strategy for hypothermia in PubMed

Concepts	PubMed search strategy	Research
Injury	"Craniocerebral Trauma"[Majr] OR (diffus* AND axonal injur*[Title/Abstract]) OR "head trauma"[Title/Abstract] OR "head injury"[Title/Abstract] OR "head injuries"[Title/Abstract] OR "brain trauma"[Title/Abstract] OR "brain injury"[Title/Abstract] OR "brain injuries"[Title/Abstract] OR "cerebral trauma"[Title/Abstract] OR "cerebral injury"[Title/Abstract] OR "cerebral injuries"[Title/Abstract] OR "craniocerebral trauma"[Title/Abstract] OR "craniocerebral injury"[Title/Abstract] OR "craniocerebral injuries"[Title/Abstract] OR "TBI"[Title/Abstract] OR "traumatic brain injury"[Title/Abstract] OR "traumatic brain injuries"[Title/Abstract] OR "brainstem trauma"[Title/Abstract] OR "brainstem injury"[Title/Abstract] OR "brainstem injuries"[Title/Abstract] OR "Head Injuries, Closed"[MeSH:NoExp] OR "Brain Injuries"[MeSH:NoExp] OR "Craniocerebral Trauma"[MeSH:NoExp] OR "Brain Hemorrhage, Traumatic"[MeSH] OR "Diffuse Axonal Injury"[MeSH:NoExp] OR "Coma, Post-Head Injury"[MeSH:NoExp] OR "Head Injuries, Penetrating"[MeSH:NoExp] OR "Intracranial Hemorrhage, Traumatic"[MeSH] OR "Skull Fractures"[MeSH]	#1
Clinical practice	"Hypothermia"[Mesh] OR "Cryotherapy"[Mesh] OR "Body Temperature"[Mesh] OR "artificial hibernation"[Title/Abstract] OR "body cooling"[Title/Abstract] OR cold*[Title/Abstract] OR cool*[Title/Abstract] OR "cooling therapy"[Title/Abstract] OR "cooling therapies"[Title/Abstract] OR cryogen*[Title/Abstract] OR cryother*[Title/Abstract] OR cryotreat*[Title/Abstract] OR hypotherm*[Title/Abstract] OR normotherm*[Title/Abstract] OR refrigeration*[Title/Abstract] OR temperature*[Title/Abstract]	#2
Filter for systematic reviews	(((systematic review[ti] OR systematic literature review[ti] OR systematic scoping review[ti] OR systematic narrative review[ti] OR systematic qualitative review[ti] OR systematic evidence review[ti] OR systematic quantitative review[ti] OR systematic meta-review[ti] OR systematic critical review[ti] OR systematic mixed studies review[ti] OR systematic mapping review[ti] OR systematic cochrane review[ti] OR systematic search and review[ti] OR systematic integrative review[ti]) NOT comment[pt] NOT (protocol[ti] OR protocols[ti])) NOT MEDLINE [subset]) OR (Cochrane Database Syst Rev[ta] AND review[pt]) OR systematic review[pt]	#3
Total	#1 AND #2 AND #3	#4

Authors' contributions:

Pier-Alexandre Tardif contributed to the elaboration of keywords, developed and tested the search strategy, drafted the manuscript and approved the final version of the manuscript.

Lynne Moore led the development of the protocol and drafted the manuscript with the first author. She acts as guarantor for the review.

François Lauzier contributed to developing keywords, validated the search strategy and the data extraction form, revised the manuscript and approved the final version.

Imen Farhat contributed to the elaboration of keywords, the search strategy and the data extraction form, critically revised and approved the final version of the manuscript.

Patrick Archambault contributed to working definitions, developed keywords, revised the manuscript and approved the final version.

François Lamontagne contributed to working definitions, developed keywords, revised the manuscript and approved the final version.

Michael Chassé validated the search strategy and the data extraction form, revised the manuscript and approved the final version.

Henry Thomas Stelfox contributed to the development of research objectives, inclusion criteria, the search strategy and the extraction form, developed keywords, revised the manuscript and approved the final version.

Belinda Gabbe elaborated inclusion and exclusion criteria and keywords, revised the manuscript and approved the final version.

Fiona Lecky elaborated inclusion and exclusion criteria and keywords, revised the manuscript and approved the final version.

John Kortbeek contributed to the development of research objectives, study definitions, inclusion criteria, and the extraction form, developed keywords, revised the manuscript and approved the final version.

Paule Lessard Bonaventure contributed to the development of research objectives and inclusion criteria, elaborated keywords, validated the data extraction form, critically revised the manuscript and approved the final version.

Catherine Truchon elaborated inclusion and exclusion criteria and keywords, contribution to the development of the conceptual framework and concept definitions, revised the manuscript and approved the final version.

Alexis F. Turgeon elaborated inclusion criteria and clinically significant outcomes, validated the search strategy, elaborated keywords, revised the manuscript and approved the final version.

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Competing interests statement: None of the authors have any conflicts of interest to declare.

Word Count: 1484 words.

PRISMA-P 2015 Checklist

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	X	☐	1-2
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	☐	X	NA
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	X	☐	76-77
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	X	☐	4-51
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	X	☐	330-362
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	☐	X	NA
Support					
Sources	5a	Indicate sources of financial or other support for the review	X	☐	364-370
Sponsor	5b	Provide name for the review funder and/or sponsor	X	☐	360-363
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	X	☐	364
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	X	☐	89-118
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	X	☐	117-118 150-151
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	X	☐	129-142
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	X	☐	148-155
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned	X	☐	149-151

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
		limits, such that it could be repeated			
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	X	☐	157-177
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	X	☐	157-165
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	X	☐	167-177
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	X	☐	150-151 167-177
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	X	☐	150-151 167-177
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	X	☐	179-182
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☐	X	NA
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)	☐	X	NA
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	☐	X	NA
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	X	☐	189-193
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	☐	X	NA
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	X	☐	184-187

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Low-value clinical practices in adult traumatic brain injury: an umbrella review protocol

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Keywords:	Low-value clinical practices, traumatic brain injury, umbrella review

LOW-VALUE CLINICAL PRACTICES IN ADULT TRAUMATIC BRAIN INJURY: AN UMBRELLA REVIEW PROTOCOL

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Keywords: Low-value clinical practices, traumatic brain injury, umbrella review

Running head: Umbrella review on low-value practices in acute TBI care

ABSTRACT

Introduction: Traumatic brain injury (TBI) leads to 50,000 deaths, 85,000 disabilities and costs $60 billion each year in the USA. Despite numerous interventions and treatment options, the outcomes of TBI have improved little over the last three decades. In a previous scoping review and expert consultation survey, we identified 15 potentially low-value clinical practices in acute TBI. The objective of this umbrella review is to synthesise the evidence on potentially low-value clinical practices in the care of acute TBI.

Methods and analysis: Using umbrella review methodology, we will search Cochrane CENTRAL, EMBASE, Epistemonikos, PROSPERO and PubMed to identify systematic reviews evaluating the effect of potential intra-hospital low-value practices using tailored PICOS questions based on the results of a previous scoping review. We will present data on the methodological quality of these reviews (AMSTAR-2), reported effect sizes and the strength of evidence (GRADE).

Ethics and dissemination: Ethics approval is not required as original data will not be collected. Knowledge users from five healthcare quality organisations and clinical associations are involved in the design and conduct of the study. Results will be disseminated in a peer-reviewed journal, at international scientific meetings and to clinical, healthcare quality and patient-partner associations. This work will support the development of metrics to measure the use of low-value practices, inform policy makers on potential targets for de-implementation, and in the long term reduce the use of low-value clinical practices in acute TBI care.

Registration details: The protocol has been registered with the International Prospective Register of Systematic Reviews (PROSPERO, CRD42019132428).

STRENGTHS AND LIMITATIONS OF THIS STUDY

- State-of-the-art synthesis of evidence on low-value clinical practices in the care of acute TBI
- Represents a crucial step towards the de-implementation of low-value practices in acute TBI care
- Adopts an integrated knowledge translation model to ensure the results are relevant to decision makers
- For feasibility reasons, our synthesis is restricted to systematic reviews published in English since 1990
- The scope of review and the inclusion of systematic reviews precludes meta-analysis

INTRODUCTION

Traumatic brain injury (TBI) is the main cause of mortality from injury in people under 45 years of age[1] and it leads to approximately US$60 and €33 billion in total medical costs in the USA[2] and Europe[3] each year, respectively. Moreover, outcomes following TBI have not improved significantly in the last four decades.[4, 5] Intervention and treatment options for TBI are multiple, but many lack robust evidence of their effectiveness.[6, 7]

Low-value clinical practices, defined as a test or procedure that is not supported by evidence and/or could expose patients to unnecessary harm [8-15] consume up to 30% of healthcare budgets.[9, 16] In the past decade, the medical community has turned towards the de-implementation of low-value practices as a promising means to reduce the strain on healthcare budgets, free-up resources and reduce harm to patients.[17] Physicians report using low-value practices because of a lack of alternative treatment options, fear of legal consequences but also because of lack of guidelines on low-value care.[15, 18] The *Brain Trauma Foundation*, among others, publish guidelines on TBI care.[19] However, emphasis is on practices that should be adhered to rather than practices that should be avoided. *Choosing Wisely* publish recommendations specifically targeting low-value practices but few pertain to TBI care and many are based uniquely on expert consensus.[11] A previous scoping review and expert consultation survey identified 13 potentially low-value clinical practices in acute TBI care.[20] These practices represent potential targets for guidelines, overuse metrics and de-implementation interventions. However, before recommendations can be made, we need to synthesise the evidence base for these practices.

Interventions and treatment options for acute TBI have been the subject of multiple systematic reviews.[21, 22] Given this large body of available evidence, evidence maps have previously been used to summarize evidence from systematic reviews on acute TBI interventions.[7, 23] However, these evidence maps were not designed to target low-value practices and focused on moderate to severe TBI when the mild TBI population represent great potential for reducing low-value care. In addition, previous reviews have not provided a synthesis of effect sizes or strength of evidence. The objective of the present study is to synthesise the evidence on potentially low-value intra-hospital clinical practices in acute adult TBI.

METHODS AND ANALYSIS

Given the multitude of systematic reviews available for the clinical practices identified as potentially low-value (over 60 were identified in our scoping review), we opted to conduct an umbrella review (a systematic review of systematic reviews).[20] While the former aimed to fill a knowledge gap on medical overuse for acute injury care by identifying all potential low-value clinical practices, the latter will synthesise the evidence on the low-value practices pertaining to TBI. The review will be conducted according to published guidelines.[24-26] In the absence of reporting guidelines for umbrella reviews, we will use the applicable Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P).[27] The protocol has been registered with the International Prospective Register of Systematic Reviews (PROSPERO, CRD42019132428).

Eligibility criteria

The project steering committee comprising clinicians (2 emergency physicians, 7 critical care physicians, 1 neurosurgeon), methodologists (4), and health system managers (3) used the population, intervention, comparator, outcome and study design (PICOS) framework to develop specific research questions for each potentially low-value clinical practice (Table 1).[20, 28] We will consider systematic reviews of original studies evaluating the effectiveness of pre-determined clinical practices in acute TBI in adults (≥ 16 years old), without restriction on location of publication but limited to studies published in English since 1990.[25, 26]

We will use the Cochrane definition to identify systematic reviews. We will consider a review to be systematic if it clearly stated a set of objectives and reported explicit eligibility criteria, an extensive search strategy (a refined search strategy ran on MEDLINE or Cochrane Library and at least one other database)[29, 30] and reproducible methods to identify, select, and critically appraise the findings of the included studies.[24]

Outcomes

Primary and secondary outcomes were identified for each of the evaluated clinical practices by the project steering committee and are described in a PICO format in Table 1.

Search strategy

In consultation with an information specialist, we will develop comprehensive literature search strategies separately for each clinical practice to be studied (see Table 2 for a preliminary search strategy in PubMed). We will search systematic reviews using the Cochrane Library, Excerpta Medica Database (EMBASE), Epistemonikos,[31] PubMed and the International Prospective Register of Systematic Reviews (PROSPERO)[32] from 1990 to up to six months prior to submission for publication. Using a snowball approach, we will screen the references of included studies in addition to previous reviews on this subject.[7, 21-23, 33]

Selection process

We will manage all citations with EndNote software (version X8.2, Clarivate Analytics, 2014). We will identify and remove duplicates using electronic and manual screening.[34] To ensure reliability when selecting studies for a given practice, two sets of 100 citations will independently be evaluated and then discussed by the reviewers. Pairs of reviewers (PAT, LM, IF, KMB) will then independently screen all identified records using titles, abstracts and full texts, consecutively. Any disagreement will be resolved through discussion between reviewers and, if necessary, consultation with a senior author (AFT). Potentially eligible studies excluded using full texts will be described in a PRISMA flow chart.

Data items and abstraction process

Using a standardized data abstraction form piloted on a representative sample of 5 studies, pairs of experienced reviewers (PAT, LM, IF, KMB) will independently extract the following data: first author, title, year of publication, databases used and date of the last search; population(s), intervention(s), comparator(s), outcome(s) and study designs included; measures of association and their respective measure of heterogeneity; tools used to assess the quality (risk of bias) of original studies and overall rating from the authors. Any disagreement will be resolved through discussion between reviewers and, if necessary, consultation with a senior author (AFT). When information is available in figures only, we will abstract graphical data using computer-assisted software.[35, 36] Furthermore, we will contact study authors (up to three email attempts) when information is unclear or unavailable.

Methodological quality assessment

Two reviewers (PAT, LM) will independently critically appraise the quality of systematic reviews using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR-2) tool.[37] Methodological quality will be categorised as low (0-3), medium (4-7) and high (8-11).

Synthesis

Results will be presented according to current recommendations for umbrella reviews.[38] For each low-value practice, we will present the number of studies, study designs, and patients included, the quality of the reviews (AMSTAR-2), effect sizes for primary and secondary outcomes (forest plots) and strength of recommendations (GRADE).

Potential limitations

To ensure the feasibility of the review, we will restrict our search to low-value practices identified in the scoping review and expert consultation study, which may lead us to miss some low-value practices. However, given the robust search strategy used in our scoping review and the fact that experts were asked to add any other practices they considered low-value, it is unlikely that important low-value practices have been missed. By targeting systematic reviews rather than original studies, we may miss some evidence. However, given the availability of high-quality, up-to-date reviews in TBI care suggested by our scoping review, we think it unlikely that we will miss a large body of evidence. For certain clinical practices, we may not identify any high-quality, up-to-date reviews. These practices will be the subject of systematic reviews in subsequent phases of the research program. Finally, for feasibility reasons, we limited this umbrella review to reviews published in English since 1990 as per recommendations for umbrella reviews.[25, 26] These limitations should have negligible impact on results since few systematic reviews were published prior to 1990 and most published reviews are likely to be written in English.[25, 26]

Potential impact

This review is part of the *Canadian Program on Monitoring Low-Value Clinical Practices in Injury Care* (Canadian Institutes of Health Research #113664), aiming to evaluate the effectiveness of an audit-feedback module targeting low-value clinical practices in acute injury care. The results of

this review will be used to inform the development of quality indicators to be integrated in the audit-feedback module.

We will use state-of-the-art methods to optimize the sensitivity of our search strategy and the robustness of results. Results will be synthesised graphically. Ultimately, this research will inform the development of metrics, guidelines and de-implementation interventions, all targeting low-value injury care. The reduction of low-value clinical practices in acute TBI care has the potential to reduce pressure on strained healthcare budgets, free up resources, reduce adverse events and improve patient outcomes.

ETHICS AND DISSEMINATION

Ethics approval is not required as original data will not be collected. This study will be disseminated in a peer-reviewed journal, international scientific meetings, to knowledge users through clinical and healthcare quality associations (Choosing Wisely Canada, Trauma Association of Canada, American College of Surgeons – Committee on Trauma, International Federation of Emergency Medicine, Institut national d'excellence en santé et en services sociaux, Brain Trauma Foundation) and to patient partners associations (Brain Injury Canada).

Patient and Public Involvement

No patient or public representatives will be involved in this study.

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Tables

Table 1. PICOS for each clinical practice

#	Clinical practice
	Mild traumatic brain injury
1	*Population*: adults with acute mild traumatic brain injury *Intervention*: validated clinical decision rule (e.g. CCHR, CHIP, NEXUS II, NOC) *Comparator*: none *Primary Outcome*: false negative rate (intracranial injury, neurosurgical intervention) *Secondary Outcomes*: sensitivity, specificity *Study design*: systematic review
2	*Population*: adults with acute mild complicated traumatic brain injury *Intervention*: routine repeat head CT in absence of neurological deterioration *Comparator*: none or no repeat head CT in absence of neurological deterioration *Primary Outcome*: progression of intracranial injury *Secondary Outcomes:* neurosurgical intervention, mortality, change in management, hospital length of stay *Study design*: systematic review
3	*Population*: adults with acute mild traumatic brain injury and on anticoagulant and/or antiplatelet therapy *Intervention*: : routine repeat head CT in absence of neurological deterioration *Comparator*: none or no repeat head CT in absence of neurological deterioration *Primary Outcome*: progression of intracranial injury *Secondary Outcomes:* neurosurgical intervention, mortality, change in management, hospital length of stay *Study design*: systematic review
4	*Population*: adults with acute mild traumatic brain injury who are negative on head CT *Intervention*: neurosurgical consultation *Comparator*: none or no neurosurgical consultation *Primary Outcome*: hospital admission *Secondary Outcomes:* neurosurgical intervention, mortality, ICU admission, repeat head CT, hospital length of stay *Study design*: systematic review
5	*Population*: adults with acute mild complicated traumatic brain injury who are not on irreversible anticoagulation *Intervention*: intensive care unit admission

	Comparator: admission to regular ward or step-down unit *Primary Outcome*: neurological/medical decline, neurosurgical intervention *Secondary Outcomes:* medical interventions, mortality, adverse events, hospital length of stay, discharge destination *Study design*: systematic review
	Moderate and severe traumatic brain injury
6	*Population*: adults with acute traumatic brain injury on antiplatelet therapy *Intervention*: platelet transfusion *Comparator*: no platelet transfusion *Primary Outcome*: GOS or GOS-E *Secondary Outcomes:* mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review
7	*Population*: adults with basal skull fractures without evidence of cerebrospinal fluid leakage *Intervention*: antibiotic prophylaxis *Comparator*: no antibiotic prophylaxis *Primary Outcome*: meningitis (confirmed by lumbar puncture) *Secondary Outcomes:* GOS or GOS-E, mortality, surgical correction in patients with CSF leakage, non-CNS infection, hospital and ICU length of stay *Study design*: systematic review
8	*Population*: adults with acute traumatic brain injury and no refractory intracranial hypertension *Intervention*: therapeutic hypothermia *Comparator*: no therapeutic hypothermia *Primary Outcome*: GOS or GOS-E *Secondary Outcomes:* intracranial pressure, mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review
9	*Population*: adults with acute traumatic brain injury *Intervention*: antibiotic prophylaxis for external ventricular drain placement *Comparator*: no antibiotic prophylaxis *Primary Outcome*: ventriculostomy-related infection *Secondary Outcomes:* GOS, mortality, hospital and ICU length of stay *Study design*: systematic review
10	*Population*: adults with acute traumatic brain injury and no refractory intracranial hypertension *Intervention*: neuromuscular blocking agents

	Comparator: no neuromuscular blocking agents *Primary Outcome*: GOS or GOS-E *Secondary Outcomes:* intracranial pressure, mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review
11	*Population*: adults with acute traumatic brain injury *Intervention*: plasma transfusion *Comparator*: no plasma transfusion *Primary Outcome*: GOS or GOS-E *Secondary Outcomes:* mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review
	Severe traumatic brain injury
12	*Population*: adults with acute severe traumatic brain injury *Intervention*: albumin *Comparator*: any other colloid-containing fluids (dextrans, modified gelatins, hydroxyethyl starches) or isotonic crystalloid fluids (saline 0.9% and balanced salt solutions such as compound sodium lactate, Plasma-Lyte) *Primary Outcome*: GOS or GOS-E *Secondary Outcomes:* mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review
13	*Population*: adults with acute severe traumatic brain injury *Intervention*: antiseizure prophylaxis (levetiracetam or phenytoin) >1 week *Comparator*: antiseizure prophylaxis <1 week or no antiseizure prophylaxis *Primary Outcome*: late post-traumatic seizure *Secondary Outcomes:* GOS or GOS-E, mortality, adverse events, hospital and ICU length of stay *Study design*: systematic review

CCHR, Canadian Computed Tomography Head Rule; CHIP, Computed Tomography in Head Injury Patients; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; GOS, Glasgow Outcome Scale; ICU, intensive care unit; NEXUS, National Emergency X-Radiography Utilisation Study; NOC, New Orleans Criteria

Table 2. Search strategy for hypothermia in PubMed

Concepts	PubMed search strategy	Research
Injury	"Craniocerebral Trauma"[Majr] OR (diffus* AND axonal injur*[Title/Abstract]) OR "head trauma"[Title/Abstract] OR "head injury"[Title/Abstract] OR "head injuries"[Title/Abstract] OR "brain trauma"[Title/Abstract] OR "brain injury"[Title/Abstract] OR "brain injuries"[Title/Abstract] OR "cerebral trauma"[Title/Abstract] OR "cerebral injury"[Title/Abstract] OR "cerebral injuries"[Title/Abstract] OR "craniocerebral trauma"[Title/Abstract] OR "craniocerebral injury"[Title/Abstract] OR "craniocerebral injuries"[Title/Abstract] OR "TBI"[Title/Abstract] OR "traumatic brain injury"[Title/Abstract] OR "traumatic brain injuries"[Title/Abstract] OR "brainstem trauma"[Title/Abstract] OR "brainstem injury"[Title/Abstract] OR "brainstem injuries"[Title/Abstract] OR "Head Injuries, Closed"[MeSH:NoExp] OR "Brain Injuries"[MeSH:NoExp] OR "Craniocerebral Trauma"[MeSH:NoExp] OR "Brain Hemorrhage, Traumatic"[MeSH] OR "Diffuse Axonal Injury"[MeSH:NoExp] OR "Coma, Post-Head Injury"[MeSH:NoExp] OR "Head Injuries, Penetrating"[MeSH:NoExp] OR "Intracranial Hemorrhage, Traumatic"[MeSH] OR "Skull Fractures"[MeSH]	#1
Clinical practice	"Hypothermia"[Mesh] OR "Cryotherapy"[Mesh] OR "Body Temperature"[Mesh] OR "artificial hibernation"[Title/Abstract] OR "body cooling"[Title/Abstract] OR cold*[Title/Abstract] OR cool*[Title/Abstract] OR "cooling therapy"[Title/Abstract] OR "cooling therapies"[Title/Abstract] OR cryogen*[Title/Abstract] OR cryother*[Title/Abstract] OR cryotreat*[Title/Abstract] OR hypotherm*[Title/Abstract] OR normotherm*[Title/Abstract] OR refrigeration*[Title/Abstract] OR temperature*[Title/Abstract]	#2
Filter for systematic reviews	(((systematic review[ti] OR systematic literature review[ti] OR systematic scoping review[ti] OR systematic narrative review[ti] OR systematic qualitative review[ti] OR systematic evidence review[ti] OR systematic quantitative review[ti] OR systematic meta-review[ti] OR systematic critical review[ti] OR systematic mixed studies review[ti] OR systematic mapping review[ti] OR systematic cochrane review[ti] OR systematic search and review[ti] OR systematic integrative review[ti]) NOT comment[pt] NOT (protocol[ti] OR protocols[ti])) NOT MEDLINE [subset]) OR (Cochrane Database Syst Rev[ta] AND review[pt]) OR systematic review[pt]	#3
Total	#1 AND #2 AND #3	#4

Authors' contributions:

Pier-Alexandre Tardif contributed to the elaboration of keywords, developed and tested the search strategy, drafted the manuscript and approved the final version of the manuscript.

Lynne Moore led the development of the protocol and drafted the manuscript with the first author. She acts as guarantor for the review.

François Lauzier contributed to developing keywords, validated the search strategy and the data extraction form, revised the manuscript and approved the final version.

Imen Farhat contributed to the elaboration of keywords, the search strategy and the data extraction form, critically revised and approved the final version of the manuscript.

Patrick Archambault contributed to working definitions, developed keywords, revised the manuscript and approved the final version.

François Lamontagne contributed to working definitions, developed keywords, revised the manuscript and approved the final version.

Michael Chassé validated the search strategy and the data extraction form, revised the manuscript and approved the final version.

Henry Thomas Stelfox contributed to the development of research objectives, inclusion criteria, the search strategy and the extraction form, developed keywords, revised the manuscript and approved the final version.

Belinda Gabbe elaborated inclusion and exclusion criteria and keywords, revised the manuscript and approved the final version.

Fiona Lecky elaborated inclusion and exclusion criteria and keywords, revised the manuscript and approved the final version.

John Kortbeek contributed to the development of research objectives, study definitions, inclusion criteria, and the extraction form, developed keywords, revised the manuscript and approved the final version.

Paule Lessard Bonaventure contributed to the development of research objectives and inclusion criteria, elaborated keywords, validated the data extraction form, critically revised the manuscript and approved the final version.

Catherine Truchon elaborated inclusion and exclusion criteria and keywords, contribution to the development of the conceptual framework and concept definitions, revised the manuscript and approved the final version.

Alexis F. Turgeon elaborated inclusion criteria and clinically significant outcomes, validated the search strategy, elaborated keywords, revised the manuscript and approved the final version.

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Word Count: 1494 words.

PRISMA-P 2015 Checklist

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	X	☐	1-2
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	☐	X	NA
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	X	☐	76-77
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	X	☐	4-51
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	X	☐	339-371
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	☐	X	NA
Support					
Sources	5a	Indicate sources of financial or other support for the review	X	☐	373-377
Sponsor	5b	Provide name for the review funder and/or sponsor	X	☐	373-377
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	X	☐	377
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	X	☐	87-116
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	X	☐	115-116 146-147
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	X	☐	130-137
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	X	☐	148-155
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned	X	☐	149-156

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
		limits, such that it could be repeated			
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	X	☐	158-177
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	X	☐	158-166
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	X	☐	168-178
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	X	☐	145-147 168-178
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	X	☐	145-147 168-178
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	X	☐	180-183
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☐	X	NA
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)	☐	X	NA
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	☐	X	NA
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	X	☐	185-189
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	☐	X	NA
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	X	☐	185-189